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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------------------|-----------------------------|
| 10/510,272 | 10/05/2004 | Charles Howard Mitch | X-15578 | 1629 |
| 25885 7590 05/02/2007 ELI LILLY & COMPANY PATENT DIVISION P.O. BOX 6288 INDIANAPOLIS, IN 46206-6288 | | | EXAMINER CHANG, CELIA C | |
| | | | ART UNIT 1625 | PAPER NUMBER |
| | | | NOTIFICATION DATE 05/02/2007 | DELIVERY MODE ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

| | | | |
|------------------------------|-------------------------------|------------------------------|--|
| Office Action Summary | Application No. 10/510,272 | Applicant(s) MITCH ET AL. | |
| | Examiner Celia Chang | Art Unit 1625 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Amendment and response filed by applicants dated Sept. 20, 2006 have been entered and considered carefully.

Claims 4-12 have been canceled. Claim 13 has been added. Claims 1-3, 13 are pending.

2. The objection and rejections of claims 4-12 of record are dropped in view of the cancellation of the claims.

3. The rejection of claims 1-3 under 35 USC 103(a) over Mitch et al. in view of Armer et al. '592 is maintained and now also applicable to newly added claim 13.

Initially, it was observed that the allegation that the Armer et al. '592 reference does not teach cycloalkyl substitution at the piperidine nitrogen is erroneous. Applicants' attention is drawn to p. 29 claim 1, lines 45-47, one of the option for this moiety is alkyl substituted by hydroxyl and terminated with a C₃₋₈cycloalkyl, thus, generically encompassed the cyclohexyl of the instant claim.

Applicants' argument that the specification provided description that the instantly claimed compounds are "at least 2 fold..." or "comparable potency...." Or exhibits a "significantly reduced *potential* for inhibiting the cytochrome P450....", thus, such data offered rebuttal to a prima facie case of obviousness.

Please note that table 1 of page 16 provided binding activity of the different opioid receptor subtypes. No statistics or any significant level can be found as to show that the compounds are actually significantly different in their binding specificity. As a matter of fact, the "profile" of the three compound showed similar selectivity among the three subtypes in similar manner. Different compounds have different binding value which is expected. The court has set forth that mere superiority or potency among different compounds is not unexpectancy. See In re Soni 34 USPQ2d; or In re Merck 231 USPQ 375 at 381:

"The core of it is that, while there are some differences in degree between the properties of amitriptyline and imipramine, the compounds expectedly have the same type of biological activity. In the absence of evidence to show that the properties of the compounds differed in such an appreciable degree that the difference was really unexpected . . . appellants' evidence was insufficient to rebut the prima facie case. The

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fact that amitriptyline and imipramine, respectively, helped some patients and not others does not appear significant. As noted by the Board, a difference in structure, although slight, would have been expected to produce some difference in activity.”

Therefore, mere better binding without competent statistical evaluation employing polulation does not offer unexpectency in rebuttal an established prima facie case of obviousness.

4. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

A survey of the specification indicated that nowhere was it disclosed what kind of solvate the compound can form nor any known solvent that will form a solvate with the compound or any solvate or hydrate being made.

Claim 1 newly amended is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A survey of the specification no process of how a solvate can be made is disclosed or any solvate was made.

Unlike pharmaceutically acceptable addition salt of an organic base compound of the claim which is a natural extension in derivatization after the compound has been made; the formation of solvate is not an automatic extension in derivatization after the compound has been obtained. As a matter of fact, the chemical field recognized the extreme unpredictability of obtaining a solvate with a known compound. It was recognized that (see Braga p.3640) “...solvate formation can be a nightmare, because it is extremely difficult to predict...”. Therefore, absent of any teaching or guidance that which solvents, under what conditions, forming what solvate, the scope encompassing “solvate” thereof lacks sufficient enabling disclosure.

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5. Applicants' amendment necessitated the new grounds of rejection.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

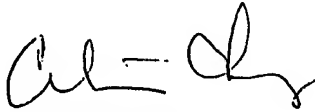
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie, Ph. D., can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Apr. 24, 2007


Celia Chang
Primary Examiner
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